REMARKS

Claims 1-3, 6, 7, 17-19, 38, 53, and 57-59 were previously pending and examined in this application. By this amendment, claims 6 and 53 have been canceled and claims 1-3 and 7 have been amended. As a result, claims 1-3, 7, 17-19, 38, and 57-59 are pending for examination.

Claims 1 and 2 were amended to recite that the claimed nucleic acid molecule comprises or consists of SEQ ID NO:4, respectively. Claim 3 was amended to depend from claim 1 in view of the amendments to claims 1 and 2. Claims 1 and 7 were amended to recite that the complements are "full-length" complements. Support for the amendments is provided in the specification and claims as filed. No new matter has been added.

Applicant respectfully requests withdrawal of the finality of the rejection, because the Examiner has raised a new rejection that was not necessitated by an amendment to the claims in the previous response. See the response to the first enablement rejection on page 8 below.

Rejections Under 35 U.S.C. § 112, First Paragraph

Written description rejections

The Examiner has maintained the rejection of claims 1, 7, 17-19, 38, 53 and 57-59 under 35 U.S.C. § 112, first paragraph as lacking an adequate written description. Applicant has amended the claims with respect to the full-length of complements and to remove the hybridization language from claim 1. These amendments obviate the Examiner's objections, particularly with respect to an alleged lack of certainty in the function of sequences that hybridize to the 137 nt probe described in the specification (although this was not claimed).

Applicant notes that claim 1 now covers an isolated nucleotide sequence that comprises SEQ ID NO:4. Applicants wish to draw the Examiner's attention to the USPTO's Revised Interim Written Description Guidelines Training Materials, particularly Example 8, which covers a factual situation analogous to Applicant's specification and claim 1. For convenience, Example 8 is reproduced below:

Example 8: DNA fragment Encoding a Full Open Reading Frame (ORF)

Specification: The specification discloses that a cDNA library was prepared from human kidney epithelial cells and 5000 members of this library were sequenced and open reading frames were identified. The specification discloses a Table that indicates that one member of the library having SEQ ID NO: 2 has a high level of homology to a DNA ligase. The specification teaches that this complete ORF (SEQ ID NO: 2) encodes SEQ ID NO: 3. An alignment of SEQ ID NO: 3 with known amino acid sequences of DNA ligases indicates that there is a high level of sequence conservation between the various known ligases. The overall level of sequence similarity between SEQ ID NO: 3 and the consensus sequence of the known DNA ligases that are presented in the specification reveals a similarity score of 95%. A search of the prior art confirms that SEQ ID NO: 2 has high homology to DNA ligase encoding nucleic acids and that the next highest level of homology is to alpha-actin. However, the latter homology is only 50%. Based on the sequence homologies, the specification asserts that SEQ ID NO: 2 encodes a ligase.

Claim 1: An isolated and purified nucleic acid comprising SEQ ID NO: 2.

Analysis:

A review of the full content of the specification indicates SEQ ID NO: 2 is essential to the operation and function of the claimed invention. The specification indicates that SEQ ID NO: 2 encodes a protein that would be expected to act as a DNA ligase.

A review of the language of the claim indicates that the claim is drawn to a genus, i.e., any nucleic acid that minimally contains SEQ ID NO: 2. The claim is drawn to a nucleic acid comprising a full open reading frame. The claimed nucleic acid does not read on a genomic sequence because full length mammalian cDNAs would not be expected to contain introns or transcriptional regulatory elements such as promoters that are found in genomic DNA. The claim reads on the claimed ORF in any construct or with additional nucleic acid residues placed at either end of the ORF.

The search indicates that SEQ ID NO: 2 is a novel and unobvious sequence.

There is a single species explicitly disclosed (a molecule consisting of SEQ ID NO: 2 that is within the scope of the claimed genus).
There is actual reduction to practice of the disclosed species.
One of skill in the art can readily envisage nucleic acid sequences which include SEQ ID NO: 2 because e.g. SEQ ID NO: 2 can be readily embedded in known vectors. Although there may be substantial variability among the species of DNAs encompassed within the scope of the claim because SEQ ID NO: 2 may be combined with sequences known in the art, e.g. expression vectors, the necessary common attribute is the ORF (SEQ ID NO: 2).

> Weighing all factors including (1) that the full length ORF (SEQ ID NO: 2) is disclosed and (2) that any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession of the genus of DNAs that comprise SEQ ID NO: 2.
>
> **Conclusion:** The written description requirement is satisfied.

In view of this example and the analysis of written description contained therein, and the disclosure of Applicant's specification, Applicant asserts that claim 1 as amended is of appropriate scope and is patentable.

The Examiner stated that Applicant had not disclosed the structure of the unique fragment claimed in claim 7 (Page 7 of the Office Action: "...no disclosure is found regarding the structure of said unique fragment"). Applicants respectfully disagree, because the structural information for fragments of SEQ ID NO:4 is quite clearly provided by the sequence of SEQ ID NO:4 itself, particularly in view of the disclosure at pages 13-14 of the specification, which discloses fragments of LAGE nucleic acids.

The Examiner noted that nucleic acid sequences that comprise a fragment of SEQ ID NO:4 "remain rejected" (first sentence, page 8 of Office Action), even though there is no such claim. Without commenting on the validity of the rejection, Applicant respectfully requests that this rejection be withdrawn as not relevant to the pending claims.

The Examiner also commented that agents of claim 38 encompass "nucleotide sequences with undisclosed structure and length." Applicants disagree for the following reasons. The claim requires that the agent hybridize under a specifically defined set of conditions to a specifically defined sequence. This inherently provides the agent with a structure by virtue of its hybridization properties: unrelated sequences would not hybridize. See: USPTO Revised Interim Written Description Guidelines Training Materials, Example 9 Hybridization, the portion of which that relates to hybridization is reproduced below.

> "...a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs."

Thus, because the claim recites highly stringent hybridization conditions and a target sequence (SEQ ID NO:4), the claimed invention is adequately described.

Based on the foregoing, Applicant respectfully requests that the Examiner withdraw the rejection of claims 1, 7, 17-19, 38, 53 and 57-59 under 35 U.S.C. § 112, first paragraph.

The Examiner maintained the rejection of claim 6. This rejection is obviated in view of Applicant's cancellation of claim 6. Accordingly, withdrawal of the rejection is respectfully requested.

Enablement rejections

The Examiner has maintained the rejection of claim 53 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification. Applicant has canceled claim 53, which obviates the rejection.

Applicant notes, however, that this rejection was not necessitated by Applicant's previous amendment of the claim. The rejection for a lack of enablement of gene therapy could have been made against claim 53 as previously drawn, because the only amendment of the claim was to change the preamble from a "vaccine composition" to a "composition that induces an immune response". Accordingly, the finality of the rejection is improper and should be withdrawn.

Applicant respectfully requests withdrawal of the rejection of claim 53 under 35 U.S.C. § 112, first paragraph.

The Examiner has maintained the rejection of claims 58-59 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification. The rejection is based on the Examiner's assertions that the claims include single primer PCR, and that neither the specification nor the art

at the time the invention was made disclosed how to perform single primer PCR. Applicant respectfully disagrees.

For example, US patents 5,545,522 (see claim 1 "A process for amplifying at least one target nucleic acid sequence using a single species of primer complex") and 5,599,674 (see claims 1 and 5 pertaining to analysis of "DNA associated with the BCRA1 locus") describe the use of single primer amplification in molecular diagnostics prior to Applicant's filing date. US patent 6,379,932, filed shortly after Applicant's application, also describes single primer amplification methods. Thus, one of ordinary skill in the art knew how to practice the claimed invention, even as it relates to the use of single primer PCR.

Accordingly, Applicant respectfully requests withdrawal of the rejection of claims 58-59 under 35 U.S.C. § 112, first paragraph.

The Examiner has maintained the rejection of claims 1,7, 17-19, 38, 53 and 57-59 under 35 U.S.C. § 112, first paragraph, as not enabled by the specification. The basis for the rejection is the alleged lack of enablement for a nucleic acid that hybridizes under high stringency conditions. Applicant traverses the rejection and request reconsideration.

As noted above for the written description rejections, several of the claims have been amended or canceled, thereby obviating the rejection. The one claim that arguably would still remain rejected is claim 38. This claim is a method for diagnosis, which recites both the target molecule (SEQ ID NO:4) and the hybridization conditions that define structural/sequence parameters for an agent used in the claimed diagnostic method. One of ordinary skill in the art in the field of diagnostics would be enabled to carry out the claimed invention throughout its scope, because the only experimentation that is required, if at all, is the selection of an agent (e.g., a nucleic acid probe) that binds to SEQ ID NO:4 under the stated hybridization conditions. Such experimentation is, Applicant believes, entirely routine for the person of skill in the art.

Moreover, even such minimal and routine experimentation need not be conducted because Applicant provided a number of possible probes in the specification, such as fragments of SEQ ID NO:4, particularly those sections of the sequence that are identified as differing from SEQ ID NO:8. Applicant also provided at least one working example of a probe useful in the claimed method. Therefore, one of ordinary skill in the art would not have to conduct any

experimentation in order to practice the claimed invention, but if any experimentation were carried out to select different probes, it would be considered routine in this field.

Accordingly, Applicant respectfully requests withdrawal of the rejection of claims 1,7, 17-19, 38, 53 and 57-59 under 35 U.S.C. § 112, first paragraph.

The Examiner has maintained the rejection of claims 1 and 6 under 35 U.S.C. § 112, first paragraph as being overly broad in scope and thus not enabled by the specification. Claim 6 has been canceled, and claim 1 has been amended. The amendment of claim 1 obviates the rejection.

Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of claims 1 and 6 as not enabled.

Applicant also must disagree with the Examiner's conclusions regarding the substitution or deletion of nucleotides and the effect on amino acids in a polypeptide sequence. The statement made by the Examiner simply is too broad to be correct. For example, many substitutions of nucleotides will have no effect whatsoever on the amino acid sequence.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

Lethe et al., Applicant

John R. Van Amsterdam
Reg. No. 40,212
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2211
Telephone: (617) 720-3500

Docket No. L0461.70066US00
Date: September 15, 2003
X10/04/03